United Kingdom Clinical Pharmacy Association (UKCPA) Respiratory Group
Submission to NICE MTA on Omalizumab

Omalizumab for the treatment of severe persistent allergic asthma in children aged 6 and over and adults (review of TA133 and TA201)
Response to the Appraisal Consultation Document & Evaluation Report

The United Kingdom Clinical Pharmacy Association (UKCPA) is pleased to have the opportunity to comment on the above consultation and evaluation report on omalizumab. In our response, we will address the specific questions that are raised by the Appraisal Committee, followed by our response to the provisional recommendations of the evaluation report.

Consultation Questions:

Has all of the relevant evidence been taken into account?

The UKCPA welcomes the analysis on cost effectiveness and the steroid sparing effects of omalizumab. However, unfortunately not all significant adverse effects have been taken into account. Oral corticosteroids (OCS) are bereft with a multitude of adverse effects that blight our patients in a range of physical and mental ways. These include mental illness, skin conditions and obesity and its associated complications and conditions.

We know that chronic diseases such as severe and difficult asthma are particularly associated with a high incidence of mental health problems such as depression and anxiety. This not only has a significant impact on the individual patients quality of life and financial burden to the NHS to manage these associated conditions, but also to the patients ability to contribute to the wider society. We acknowledge and welcome the Committee's attempt to quantify many of these adverse effects, however we feel that as the effects of OCS are so profound and extensive, they should not be underestimated in terms of their effects of patients quality of life and the associated cost effectiveness of omalizumab. We therefore do not agree with the Committee's judgement that it is implausible that the unidentified or unquantified adverse effects would be significant enough to reduce the cost per QALY gained to £30,000.

We welcome the Committee's agreement that additional health-related benefits could be conferred to carers as a result of omalizumab use. While the manufacturer's submission has not included these benefits, feedback from our patients and pharmacists suggests that the impact of this is significant enough for this to be included formally in the Committee's analysis when considering omalizumab's cost effectiveness. This is true for benefits associated with parents of children with severe asthma and of carers of adults who have severe asthma.

Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

The differing interpretations in the cost effectiveness models posed by the manufacturer and the Committee have led to the differing cost per QALY gained obtained in this analysis. This has seen a reversal in the Committee's original approval for the use of omalizumab. This is despite very little information published since TA133 and TA201. Despite the differing interpretations in the cost models, the cost per QALY gained has only marginally exceeded the £30,000 threshold. This is also in view of the omission of the additional cost effectiveness that would be gained from factors that the Committee have not included in its

analysis. This includes adverse effects of long term OCS use such as obesity and depression, and the carer benefits attributed to omalizumab use.

From the limited evidence that has been published since TA133, a real world study of omalizumab use in the APEX study[1] has provided additional insights into the efficacy and associated cost effectiveness of omalizumab. As this was a study in real world setting it has the clear benefits of demonstrating which patients are being initiated on omalizumab and how it is currently being used in clinical practice. However, it also has the disadvantage of not being compared to a placebo control group. What we can see from original clinical trial data prior to TA133 and real world data from APEX since then[1], is that omalizumab is currently being used in a small and more severe cohort of patients than that originally suggested by clinical trials and TA133.

	INNOVATE[2]		**APEX**[1]
	Omalizumab (n=209)	Placebo (n=210)	Omalizumab (n=136)
Females (%)	67.5	65.7	68.0
Age years (mean)	43.4	43.3	41.0
FEV1 (% predicted) mean	61.0	61.6	66.0
Daily OCS (%)	23.4	20.0	66.2
Baseline exacerbations in preceding 12months	2.64 (37.3% reduction after 28wks)	2.41	3.67 (1.73 after 12months; 53% reduction)

The APEX study showed that patients who were given omalizumab in a real world setting tended to have a greater severity of asthma, with higher exacerbation rates prior to initiation of omalizumab, and were more likely to be on daily OCS. 66.2% of patients in the APEX study were on daily OCS compared to 23.4% in the landmark INNOVATE study[1-2]. Encouragingly, in the real world setting of APEX, 64% of patients reduced their daily OCS use with 48.5% stopping altogether[1]. This amplifies the need to ensure that all adverse effects of OCS should be included in the cost analysis as this is what is reflective of the patients that are initiated on this medicine. We are aware that patients who are usually initiated on omalizumab tend to be started on this as a last resort following years of uncontrolled asthma despite optimised therapy. This includes immunosuppressants with OCS as well as other toxic medicines such as ciclosporin. Despite these toxic therapies that have numerous adverse effects, many continue to be uncontrolled leaving omalizumab to be a last resort. The removal of this option ensures that any hope of improving their asthma control is severely minimised.

Are the provisional recommendations sound and a suitable basis for guidance to the NHS?
The provisional recommendations remove the final option available to a small, but severely affected group of patients, of ever gaining control of their asthma. In the absence of any other medicine such as this, the removal of omalizumab poses a significant impact on the equity of care for a small group of patients and their carers who have often suffered for many years with the impact of uncontrolled asthma and the significant adverse effects from medicines such as OCS and other toxic immunosuppressants. Many patients have already contacted our pharmacists in panic and distress following the provisional recommendation published by NICE, and we are aware that Asthma UK have had a similar response from patients. Consistent with the Department of Health's ethos of "no decision about me, without me", the resounding feedback from patients has been to review the provisional

recommendation not to endorse the use of omalizumab and to reverse this to a positive recommendation.

The usage of omalizumab in the UK was highlighted by NICE in 2010[3] showing that its usage has not been as high as initially estimated. This is consistent with data from the APEX study which shows that clinicians are not indiscriminately prescribing omalizumab and that only the severest of asthma patients are chosen for this expensive therapy. Furthermore, the APEX study has shown that as a result, the response rate by the small group of patients chosen to start this therapy, is higher than that seen in clinical trials, reflecting clinicians expertise in identifying the cohort that are most likely to benefit from this. Data from the manufacturer[4] suggests that only 1500 patients are prescribed this medicine, comprising of a very small proportion of the overall asthma cohort in the UK of 5.4million, or approximately 0.028%. In its analysis, the Committee has highlighted the clinical efficacy of this medicine and in view of the small group of patients for whom this medicine can genuinely transform their lives, we feel that the provisional recommendation should be changed to a positive recommendation for a small subgroup of patients.

Summary

Omalizumab is the first anti-IgE medication licensed for use in severe persistent allergic asthma. Since its introduction and approval for use by NICE, it has transformed the lives of many patients who were on optimised standard asthma therapy but who continued to have uncontrolled disease. Prior to its introduction, these patients would have otherwise had very few options, if any at all. However, in a resource limited NHS, the use of this effective but expensive therapy should only be made available in a clinical and cost effective manner.

Asthma in the UK remains to pose a significant health and societal burden, with the highest rate of self reported asthma, a rate of premature deaths that is 1.5 times higher than the rest of Europe and an annual death rate of over 1000 deaths. The Committee's analysis has shown that omalizumab is a clinically efficacious therapy in severe asthmatics. The Committee has overturned its initial positive recommendation primarily based on the cost effectiveness estimates made, which is marginally above the £30,000 threshold. In the absence of all the relevant aspects included in the cost effectiveness analysis, such as other OCS adverse effects and carer benefits, in conjunction with the higher response rate seen in real world data such as APEX, we feel that omalizumab is cost effective in a small subgroup of patients.

Based on the current evidence available and the assessment review, the UKCPA would like to urge the Committee to reconsider its provisional recommendation and to be given a positive recommendation in the following small sub group of patients where currently there are no other options for improving their asthma control or minimising the associated adverse effects of managing asthma:

- Patients should be assessed by a respiratory specialist, in a respiratory specialist centre, prior to initiating omalizumab
- Sufficient efforts should be made to ensure that patients are adherent to current asthma therapy and that a minimum of two sources of information are reviewed as part of a pre-omalizumab assessment where possible:
    - These may include asking the patient, checking prescription issue data from the GP and an adherence assessment by a pharmacist
- For use in a clearly defined group of patients who continue to suffer from severe exacerbations requiring treatment and/or admission(s) despite optimised standard asthma therapy; this group of patients includes:

    - Those who are on daily OCS
    - Or patients who are on frequent courses of OCS, irrespective of hospital admissions, defined as 4 or more acute courses of OCS over the past year
- To ensure the cost-effective use of this therapy and that the appropriate patients receive this, following the 16 week review, repeat assessments should be made at 6 monthly intervals to ensure that the patient has continued to receive benefits from this medicine and other asthma treatments are reviewed.

References:

1. The APEX study: a retrospective review of responses of severe allergic asthma patients to omalizumab in UK clinical practice. 2011.
2. Humbert M, Beasley R, Ayres J et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment); INNOVATE. Allergy 2005; 60: 309-316.
3. National Institute for Clinical Excellence. NICE implementation uptake report: Omalizumab for severe persistent allergic asthma. June 2010.
4. Novartis company information. Data on file. 2012.